

CLAIMS

WE CLAIM:

1. A method for assessing predisposition of a subject to a mental disorder phenotype having an association with an at-risk allele of a gene that encodes monoamine oxidase A enzyme, the association being conditioned by a pathogenic environmental risk factor status condition, the at-risk allele characterized by a low activity level of the enzyme in the brain of the subject, the method comprising the steps of
 - determining whether the subject carries one or more copies of an at-risk allele;
 - determining whether the subject has experienced, or is at risk of experiencing, the environmental risk factor; and
 - concluding that the subject is predisposed to the phenotype if the subject carries the at-risk allele and has experienced, or is at risk of experiencing, the environmental risk factor.
2. The method of Claim 1 wherein the subject carries the at-risk allele.
3. The method of Claim 1 wherein the subject has experienced, or is at risk of experiencing, the environmental risk factor.
4. The method of Claim 1 wherein the mental disorder phenotype is selected from the group consisting of a behavioral disorder phenotype, an emotional disorder phenotype, and a cognitive disorder phenotype wherein genetic variation in a population accounts for a high or very high proportion of total phenotypic population variation.
5. The method of Claim 1 wherein the disorder phenotype is antisocial behavior disorder.
6. The method of Claim 1 wherein the pathogenic environmental risk factor is selected from the group consisting of exposure to psychological trauma, exposure to psychosocial stress, exposure to an unhealthy diet, an infectious agent, exposure to a toxic agent, experience with a pharmacological agent, a medical trauma, and an injury.
7. The method of Claim 1 wherein the pathogenic environmental risk factor is childhood maltreatment.

8. The method of Claim 1 wherein the mental disorder phenotype is antisocial behavior disorder and the pathogenic environmental risk factor is childhood maltreatment.

9. The method of Claim 1 further comprising the step of counseling the subject to pursue or avoid a particular type of employment.

10. The method of Claim 1 further comprising the step of counseling the subject to avoid the environmental risk factor.

11. The method of Claim 1 further comprising the step of prescribing a therapy selected from the group consisting of psychological therapy and pharmaceutical therapy.

12. The method of Claim 1 wherein the step of determining whether the subject carries one or more copies of the at-risk allele comprises the steps of:

amplifying a portion of the gene using an amplification primer pair to produce an amplified fragment having a length that distinguishes the at-risk allele from another allele of the gene; and

determining whether the amplified fragment is a fragment of the at-risk allele.

13. The method of Claim 12 wherein the amplification primer pair comprises a first primer having a sequence of SEQ ID NO:1 and a second primer having a sequence of SEQ ID NO:2.

14. A method for discovering a conditional association between an allele of a gene that encodes monoamine oxidase A enzyme and a mental disorder phenotype, where the association is conditioned upon a pathogenic environmental risk factor status, the method comprising the steps of:

identifying at least one a mental disorder phenotype having high or very high heritability coefficient;

identifying a pathogenic environmental risk factor that operates on the at least one phenotype via non-genetic means and having at least higher and lower risk status conditions;

ascertaining in a population of individuals an allelic profile for the gene that encodes the enzyme having an at-risk allele characterized by a low activity level of the enzyme in the brain of the subject; and

selecting from the at least one disorder phenotype a disorder phenotype that correlates with statistical significance in the population with the at-risk allele only under the higher risk status condition, but which lacks statistically significant correlation with the at-risk allele under the lower risk status condition, whereby the at-risk allele and the mental disorder phenotype are conditionally associated with the selected disorder phenotype, the association being conditioned upon the higher environmental risk factor status condition.

15. The method of Claim 14 wherein the mental disorder phenotype is selected from the group consisting of a behavioral disorder phenotype, an emotional disorder phenotype, and a cognitive disorder phenotype wherein genetic variation in a population accounts for a high or very high proportion of total phenotypic population variation.

16. The method of Claim 14 wherein the disorder phenotype is antisocial behavior disorder.

17. The method of Claim 14 wherein the pathogenic environmental risk factor is selected from the group consisting of exposure to psychological trauma, exposure to psychosocial stress, exposure to an unhealthy diet, an infectious agent, exposure to a toxic agent, experience with a pharmacological agent, a medical trauma, and an injury.

18. The method of Claim 14 wherein the pathogenic environmental risk factor is childhood maltreatment.

19. The method of Claim 14 wherein the mental disorder phenotype is antisocial behavior disorder and the pathogenic environmental risk factor is childhood maltreatment.

20. The method of Claim 14 wherein the step of ascertaining the allelic profile comprises the steps of:

obtaining nucleic acid from the individuals in the population;

separately amplifying from the nucleic acid of the individuals a portion of the gene using an amplification primer pair to produce an amplified fragment having a length that distinguishes the at-risk allele from another allele of the gene;

determining a genotype for the individuals regarding presence of the at-risk allele; and
classifying the genotype from individuals to ascertain the allelic profile in the population.

21. The method of Claim 20 wherein the amplification primer pair comprises a first primer having a sequence of SEQ ID NO:1 and a second primer having a sequence of SEQ ID NO:2.

22. A kit comprising

a questionnaire that solicits input about a subject relevant to the subject's experience with at least one of (a) a pathogenic environmental risk factor and (b) a disorder phenotype; and

a system for obtaining from the subject a sample suitable for producing an allelic profile of a gene that encodes monoamine oxidase A enzyme.

23. The kit of Claim 22 further comprising a system for assaying the allelic profile of the gene.

24. The kit of Claim 23 wherein the system comprises an amplification primer pair that distinguishes the at-risk allele from another allele of the gene.

25. The kit of Claim 24 wherein the at-risk allele is characterized by a low activity level of the enzyme.

26. The kit of Claim 24 wherein the amplification primer pair comprises a first primer having a sequence of SEQ ID NO:1 and a second primer having a sequence of SEQ ID NO:2.